



US005863927A

United States Patent [19]

Smith et al.

[11] **Patent Number:** 5,863,927[45] **Date of Patent:** Jan. 26, 1999

[54] **DEXTROMETHORPHAN AND AN OXIDASE INHIBITOR FOR TREATING INTRACTABLE CONDITIONS**

[75] Inventors: **Richard Alan Smith**, La Jolla;
Jonathan M. Licht, San Diego, both of Calif.

[73] Assignee: **Center for Neurologic Study**, La Jolla, Calif.

[21] Appl. No.: 464,792

[22] PCT Filed: Sep. 22, 1994

[86] PCT No.: PCT/US94/10771

§ 371 Date: Sep. 19, 1996

§ 102(e) Date: Sep. 19, 1996

[87] PCT Pub. No.: WO96/09044

PCT Pub. Date: Mar. 28, 1996

[51] Int. Cl.⁶ A61K 31/44; A61K 31/265;
A61K 31/135

[52] U.S. Cl. 514/289; 514/305; 514/491;
514/649; 514/651; 514/652; 514/654

[58] Field of Search 514/289, 305,
514/491, 652, 654, 649, 651

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,316,888	2/1982	Nelson	424/127
5,166,207	11/1992	Smith	514/270
5,206,248	4/1993	Smith	514/289
5,350,756	9/1994	Smith	514/289
5,352,683	10/1994	Mayer et al.	514/289
5,366,980	11/1994	Smith	514/289
5,502,058	3/1996	Mayer et al.	514/289

OTHER PUBLICATIONS

Dickenson, A.H., "A cure for wind up: NMDA receptor antagonists as potential analgesics," *Trends in Pharm. Sci.* 11: 307-309 (1990).

Dickenson, A.H., et al., "Dextromethorphan and levorphanol on dorsal horn nociceptive neurones in the rat," *Neuropharmacology* 30: 1303-1308 (1991).

France, C.P., et al., "Analgesic Effects of Phencyclidine-Like Drugs in Rhesus Monkeys," *J. Pharmacol. Exp. Therapeutics* 250: 197-201 (1989).

Mao, J., et al., "Intrathecal treatment with dextrophan or ketamine potently reduces pain-related behaviors in a rat model of peripheral mononeuropathy," *Brain Research* 605: 164-168 (1993).

McCarthy, J.P., "Some less familiar drugs of abuse," *Med. J. Australia* 1971 (2): 1078-1081 (1971).

McQuay, H.J., et al., "Dextromethorphan for the treatment of neurophatic pain: a double-blind randomised controlled crossover trial with integral n-of-1 design," *Pain* 59: 127-133 (1994).

Tortella, F.C., et al., "Dextromethorphan and neuromodulation: old drug coughs up new activities," *Trends in Pharm. Sci.* 10: 501-507 (1989).

Zhang et al., "Dextromethorphan: Enhancing its Systemic Availability by Way of Low-dose Quinidine-mediated Inhibition of Cytochrome P4502D6," *Clin. Pharm. & Ther.* 51(6): 647-655 (1992).

Primary Examiner—Phyllis G. Spivack

Attorney, Agent, or Firm—Patrick D. Kelly; Christine M. Bellas

[57] **ABSTRACT**

Methods are disclosed for increasing the effectiveness of dextromethorphan in treating chronic or intractable pain, for treating tinnitus and for treating sexual dysfunction comprising administering dextromethorphan in combination with a therapeutically effective dosage of a debrisoquin hydroxylase inhibitor. A preferred combination is dextromethorphan and the oxidative inhibitor quinidine.

22 Claims, 1 Drawing Sheet

"DEPTO" 9695007